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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,546	02/25/2002	Rebecca E. Cahoon	BB1201 US CNT	1850

23906 7590 04/20/2004

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,546	CAHOON ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-17,19-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15,19-22 and 24* is/are rejected.

7)☒ Claim(s) *16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of the specification in the paper of 1/29/2004, is acknowledged. Claims 13-17, 19-22 and 24 are at issue and are present for examination.

Claim Objections

Claims 16 and 17 are objected to because of the following informalities:

Claims 16 and 17 are each dependent on rejected claim 13.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-15,19-22 and 24 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide that encodes a polypeptide having thiamin pyrophosphokinase activity comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any polynucleotide which encodes a polypeptide having thiamin pyrophosphokinase activity wherein the polypeptide has a sequence identity of at least 80% when compared to the amino acid sequence of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action. Applicants traverse this rejection on the following basis: Applicants submit that Nosaka et al. (J. Biol. Chem., 268:17440-17447, 1993) describes the isolation and characterization of a thiamin pyrophosphokinase gene from yeast (gi: 632717) and the expression of the yeast enzyme in *E. coli*, which lacks thiamin pyrophosphokinase activity, showed marked activity of this enzyme in the prokaryotic cell. Applicants further submit that a comparison of the claimed sequence with the yeast thiamin pyrophosphokinase and the mouse gene product (gi: 6468206) shows 18.7% and 24.3%, respectively, sequence identity and that all three sequences display essentially the same glycine-rich motif typical for nucleotide phosphate group binding and reminiscent of the Rossman fold. Applicants further submit that recent crystallographic data of the mouse enzyme identified residues of the thiamin pyrophosphokinase active site (Timm et al. JMB, Vol 310:, 195-201, 2001).

Applicants submit that the above referred to comparison demonstrates the sequence of the invention possesses stretches of highly conserved regions and that one skilled in the art would appreciate that the more highly conserved a residue is, the less likely it could be modified and function maintained and that thus one could quickly determine which amino acid residues might be modified in SEQ ID NO: 2 without a likely change in function and that since SEQ ID NO: 2 shares 18.7% and 24.32% identity with the yeast and mouse proteins, respectively one of skill in the art would have appreciated that many variants sharing at least 80% sequence identity to the SEQ ID NO: 2 would have been expected to retain thiamin pyrophosphokinase activity.

Applicants thus conclude that in view of the discussion above, one skilled in the art would have known how to use the claimed sequence without undue experimentation and that the rejection according to 35 USC 112 first paragraph should be removed.

Applicants argument is acknowledged, however, not found persuasive for the following: First applicants are reminded that all of the currently rejected claims depend from and include the limitations of claim 13 which limits the claimed polynucleotides such that they must encode a thiamin pyrophosphokinase, thus there was never a question that one of skill in the art would not know hoe to use the claimed sequence without undue experimentation. Second applicants are reminded that the claims must be enabled at the time of filing, and thus reference to crystallographic data that occurred after applicants filing date is not useful in support of applicants position.

The rejected claims are rejected based on a lack of enablement with respect to how to make the members of the claimed genus which includes any polynucleotide which encodes a thiamin pyrophosphokinase and which has a mere 80% sequence identity to SEQ ID NO: 2.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a thiamin pyrophosphokinase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue

experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide which encodes any polypeptide having thiamin pyrophosphokinase activity having the recited amino acid sequence identity (i.e. 80%), because the specification does not establish: (A) regions of the protein structure which may be modified without effecting thiamin pyrophosphokinase activity; (B) the general tolerance of thiamin pyrophosphokinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a thiamin pyrophosphokinase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the thiamin pyrophosphokinase activity, as encoded by the polynucleotide claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure, it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus which encode a polypeptide having the claimed thiamin pyrophosphokinase activity.

Conclusion

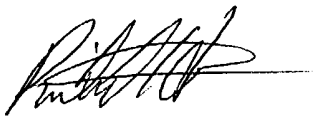
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
4/13/2004